REMARKS/ARGUMENTS

In this response, Claim 1 has been amended and new Claims 11-20 have been added. The subject matter contained in the newly-added claims are fully supported by the disclosure in the application and are not disclosed or taught by the prior art. Thus, Claims 1-2 and 11-20 remain pending in the present application.

I. Claim Rejections - 35 U.S.C. § 112, first paragraph

Claim 2 is rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Specifically, the Examiner states:

> The description is not complete since the Applicant did not describe precisely how the delivery of a non-toxic dye to the cancerous cells would kill the cells. In addition, Applicant did not describe or even suggest a dosage for using the dye as a cancer cell killer.

Office Action, dated 6/12/06, at page 3. Applicant respectfully disagrees.

Claim 2 currently recites "[a] method for selective killing of oral epithelial cancer cells in the locus of normal cells of the oral epithelium comprising the step of contacting said cancer cells with ***a cationic supravital mitochondrial marking agent other than toluidine blue O.***" Claim 2 does not recite the delivery of "a non-toxic dye" as stated by the Examiner. Moreover, there is nothing in the specification that discloses that the "supravital mitochondrial marking agent other

than toluidine blue O" includes, or for that matter excludes, "a non-toxic dye."

Applicant respectfully submits that an adequate written description for Claim 2 exists in the specification. An applicant may show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Enzo Biochem.*, 323 F.3d 956, 964 (Fed. Cir. 2002). In the Specification, Applicant discloses and describes the differences in "cell marking and killing ability" of various marking agents as a function of the structural features and describes various mechanisms of action. *See, e.g.,* Specification, at paragraphs [0026]-[0033].

For the foregoing reasons, Applicant respectfully requests that the rejection of Claim 2 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement be withdrawn.

II. Claim Rejections - 35 U.S.C. § 102(b)

Claims 1 and 2 are rejected under 35 U.S.C. § 102(b) as being anticipated by Pomerantz Edwin WO 9726018 ("Pomerantz"). Applicant respectfully disagrees.

Pomerantz, however, does not disclose ***selective marking of the mitochondria*** or ***selective killing of epithelial cancer cells*** by ***a cationic supravital mitochondrial marking agent other than toluidine blue O*** as described and claimed in Claims 1 and 2.

There is no disclosure in Pomerantz as to the **selective** staining the **mitochondria**. The Examiner points to the disclosure in Pomerantz, on page 2, line 26 bridging to page 3, line 4 with respect to toluidine blue staining of the nuclei and states that "[t]he disclosure of subcellular structures such as the nucleus includes mitochondria since both nucleus and mitochondria are subcellular structures enclosed within the cytoplasm." The disclosure in Pomerantz as to the staining of the nucleus and subcellular structures, in general, does not disclose selective marking of the mitochondria or selecting killing of the epithelial cancer cells based thereon. Moreover, this disclosure in Pomerantz, however, is limited to toluidine blue staining, which is expressly excluded from Claims 1 and 2.

In addition, Pomerantz's disclosure that toluidine blue staining "is dependent on the dye gaining access to internal subcellular structures such as the nucleus" is very different from an agent that selectively marks the mitochondria.

In fact, Applicant discloses a mechanism for the selectiveness of the staining and/or killing of the cationic supravital mitochondrial marking agent that is different from that disclosed by Pomerantz. The selective staining and/or killing of the claimed marking agent result from "the selective

update and selective retention of the agent in the mitochondria of cancer cells" and that this "uptake and retention is apparently due to the **higher electrical potential (negative charge on the inside of the membrane) of cancerous cells' mitochondria as compared to mitochondrial of normal cells.**" Specification, at para. [0015]. Applicant further states:

> In fact, the selective marking of cancer cells by, and retention in the mitochondria of cancer cells of, supravital cationic dyes and other supravital cationic marking agents, are related to one of the very characteristics of cancer cells that appears to be responsible for their rapid cloning and metastasizing ability, namely, that the higher electrical potential of the mitochondria of cancer cells is the source of cellular energy and is the driving force for ATP (adenosine triphosphate) production by the cells.

Id. There is nothing in Pomerantz which recognizes or teaches this mechanism.

Applicant respectfully requests that the rejection to Claims 1 and 2 be withdrawn because Pomerantz does not disclose or teach the selective marking of the mitochondria or killing of oral epithelial cancer cells by a cationic supravital mitochondrial marking agent other than toluidine blue O.

III. Claim Rejections - 35 U.S.C. § 103

Claims 1 and 2 are rejected under 35 U.S.C. § 103(a) as being anticipated by Pomerantz in view of Hancock et al. U.S. Patent No. 4,816,395 ("Hancock") Specifically, Examiner states that:

> It would have been obvious to a skilled artisan at the time the invention was made to modify the method

> disclosed by Pomerantz and use the same steps for treatment after combining a chemotherapeutic drug with the dye used for detection because Hancock disclosed that in case of epithelial cells treated with labeled methotrexate, the neoplastic cells which are not sensitive to the methotrexate will normally display a drug uptake which is at least 50% higher than that of normal mammary epithelial cells, usually being 300% higher, or more. The expected result would be a method for treating oral epithelial carcinomas.

Office Action, dated 6/12/06, at page 7. Applicant respectfully disagrees.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *Id.* Second, there must be a reasonable expectation of success. *Id.* Finally, the prior art references when combined must teach or suggest all the claim limitations. *Id.*

No combination of Pomerantz and Hancock disclose the invention in Claims 1 and 2 because there is no disclosure in either Pomerantz or Hancock of the selective marking of the mitochondria or killing of oral epithelial cancer cells by a cationic supravital mitochondrial marking agent other than toluidine blue O.

Hancock discloses a non-toxic assay of toxic chemotherapy drugs in mass culture of neoplastic cells from an individual patient. There is no disclosure in Hancock of using a

mitochondrial marking agent that "is selectively taken up by the mitochondria of living cancer cells and is selectively retained in cancer cells for a time sufficient to permit identification and/or killing or incapacitation thereof." Specification, para. [0008].

Because there is no combination of Pomerantz and Hancock disclose the invention in Claims 1 and 2, Applicant respectfully requests that the rejection under § 103 should be withdrawn. Reconsideration and withdrawal of the rejection is respectfully requested.

IV. Double Patenting

Claims 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,649,144. Specifically, Examiner states that:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because the two claims recite the same invention except that claim 1 in '144 recites topically delivering the supravital mitochondrial marking agent. This does not differentiate the claim from [sic] instant claim 1 because instant claim 1 does not provide a method of administering the compound; it only gives a generic concept of administering the compound without limitations.

Office Action, dated June 12, 2006, at page 8.

Applicant files herewith a terminal disclaimer, pursuant to 37 C.F.R. 1.130(b) and 1.321(c), to overcome this

rejection. Thus, Applicant respectfully requests that the rejection be withdrawn.

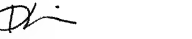
CONCLUSION

It is believed that all claims now pending patentably define the subject invention over the prior art and are in condition for allowance. Applicants respectfully request that the claims be allowed and earnestly solicit favorable action at the earliest possible date.

If any additional fees are due in this matter, please charge our Deposit Account No. 10-0440.

Respectfully submitted,

JEFFER, MANGELS, BUTLER & MARMARO LLP

Dated: December 12, 2006 By: 

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